CLAIMS

1. The use of a binary assembly comprising:

– endothelial cells with a non-angiogenic phenotype and

– endothelial cells with an angiogenic phenotype,

for the screening

of angiogenic substances vis-à-vis endothelial cells with a non-angiogenic phenotype, not substantially affecting endothelial cells with an angiogenic phenotype, or

of anti-angiogenic substances vis-à-vis endothelial cells with an angiogenic phenotype, not substantially affecting endothelial cells with a non-angiogenic phenotype.

2. The use of a binary assembly comprising:

– endothelial cells with a non-angiogenic phenotype and

– endothelial cells with an angiogenic phenotype,

for the screening of anti-angiogenic substances vis-à-vis endothelial cells with an angiogenic phenotype, not substantially affecting endothelial cells with a non-angiogenic phenotype.

3. A process for screening substances capable of inhibiting the angiogenesis of endothelial cells with an angiogenic phenotype, but not substantially affecting endothelial cells with a non-angiogenic phenotype, comprising the following stages:

– culture, on the one hand, of endothelial cells with a non-angiogenic phenotype and, on the other hand, of endothelial cells with an angiogenic phenotype, in order to respectively obtain a culture of endothelial cells with an angiogenic phenotype and a culture of endothelial cells with a non-angiogenic phenotype,

– addition, to each of the cultures defined above, of a mitogenic factor, in particular chosen from the family of the factors FGF, PDGF, VEGF or EGF, and being in particular VEGF, and of the substance to be tested, capable of inhibiting angiogenesis, and the maintenance of the abovementioned cells in culture for a time sufficient for at least one cell division cycle to occur,

– comparison of the inhibition, by the substance to be tested, of the mitogenic action of the mitogenic factor, on the one hand on the endothelial cells with an angiogenic phenotype and, on the other hand, on the endothelial cells with a non-angiogenic phenotype, making it possible to select from the abovementioned substances to be tested what inhibits the proliferation of endothelial cells with an angiogenic phenotype, but does not inhibit the proliferation of endothelial cells with a non-angiogenic phenotype.

4. A binary assembly comprising:

– endothelial cells with a non-angiogenic phenotype and

– endothelial cells with an angiogenic phenotype,

characterized in that the endothelial cells with a non-angiogenic phenotype have at least one of the following properties:

– they remain confluent when they are brought into the presence of the growth factor VEGF, without forming tubules,

– they do not proliferate under the action of VEGF,

– they are not protected from apoptosis by VEGF,

and in that the endothelial cells with an angiogenic phenotype have at least one of the following properties:

– they form tubes when they are brought into the presence of the growth factor VEGF in a collagen gel,

– they proliferate under the action of VEGF,

– they are protected from apoptosis by VEGF.

5. The endothelial cells with a non-angiogenic phenotype as defined in claim 4.

6. The endothelial cells with an angiogenic phenotype as defined in claim 4.

7. The endothelial cells of claim 5 or 6, characterized in that these are endothelial cells of vessels, in particular endothelial cells of the aorta, adrenal cortex, skin, cerebrum, retina, veins or umbilical cord artery.

8. A process for preparing endothelial cells with a non-angiogenic phenotype according to claim 5, characterized in that it comprises the following stages:

– incubation of endothelial cells, in particular removed from an aorta, in a medium containing neither oestradiol, nor growth factor, in particular VEGF, in order to obtain clones of endothelial cells with a non-angiogenic phenotype,

– removal of a clone using a micropipette, from the abovementioned clones of endothelial cells with a non-angiogenic phenotype, and the culture of this clone until cell confluence is obtained, verified by examination using a phase contrast microscope.

– selection of endothelial cells with a non-angiogenic phenotype, by verification of the phenotype of the cells obtained in the preceding stage, using the proliferation and/or migration and/or *in vitro* angiogenesis test.

9. A process for preparing endothelial cells with an angiogenic phenotype according to claim 6, characterized in that it comprises the following stages:

– incubation of endothelial cells, in particular removed from an aorta in a medium containing oestradiol and a growth factor, in particular VEGF, in order to obtain clones of endothelial cells with an angiogenic phenotype,

– removal of a clone using a micropipette, from the abovementioned clones of endothelial cells with an angiogenic phenotype, and the culture of this clone until cell confluence is obtained,

– selection of the endothelial cells with an angiogenic phenotype, by verification of the phenotype of the cells obtained in the preceding stage, using proliferation, migration or *in vitro* angiogenesis tests.

10. A polyclonal or monoclonal antibody directed against endothelial cells with an angiogenic phenotype according to claim 6, in particular a monoclonal antibody capable of activating or inhibiting angiogenesis.

11. A polyclonal or monoclonal antibody directed against endothelial cells with a non-angiogenic phenotype according to claim 5, in particular a monoclonal antibody capable of activating or inhibiting angiogenesis.

12. The monoclonal antibody of claim 10, having the following characteristics:

– it binds to the surface of endothelial cells with an angiogenic phenotype, and

– it recognizes a unit present exclusively on endothelial cells with an angiogenic phenotype, in particular a membrane receptor.

13. A process for preparing a monoclonal antibody according to claim 10, capable of activating angiogenesis, characterized in that it comprises the following stages:

– immunization of an animal by injection of cells with an angiogenic phenotype,

– fusion between myelomas of an animal and splenocytes of an animal in order to obtain hybridomas,

– culture of the hybridomas thus obtained,

– cloning of hybridomas, chosen from those obtained in the preceding stage and secreting antibodies against cells with an angiogenic phenotype,

– verification of the angiogenesis-activation properties of the abovementioned antibodies vis-à-vis angiogenic cells, in particular using the proliferation and/or migration and/or *in vitro* angiogenesis test.

14. A process for preparing a monoclonal antibody according to claim 10, capable of inhibiting angiogenesis, characterized in that it comprises the following stages:

– immunization of an animal by injection of cells with an angiogenic phenotype,

– fusion between myelomas of an animal and splenocytes of an animal in order to obtain hybridomas,

– culture of the hybridomas thus obtained,

– cloning of hybridomas, chosen from those obtained in the preceding stage and secreting antibodies against cells with an angiogenic phenotype,

– verification of the angiogenesis-inhibiting properties of the abovementioned antibodies vis-à-vis angiogenic cells, in particular using the proliferation and/or migration and/or *in vitro* angiogenesis test.

15. Anti-idiotypic antibodies directed against monoclonal antibodies themselves directed against endothelial cells with a non-angiogenic phenotype according to claim 5, or against monoclonal antibodies themselves directed against endothelial cells with an

angiogenic phenotype according to claim 6, characterized in that they are capable of activating or inhibiting the functions performed (activation or inhibition of the angiogenesis) by the antibodies according to one of claims 10 to 12.

16. Fab fragments of the monoclonal or polyclonal antibodies according to one of claims 10 to 12, and anti-idiotypic antibodies according to claim 15, said fragments being capable of activating or inhibiting angiogenesis.

17. A complex between:

– an antibody, as defined above, or a Fab fragment, angiogenesis activator, according to claim 16, and

– a radioactive element such as iodine 125 or 131, indium, yttrium or any other compound containing an ionizing particle.

18. A complex between an antibody according to one of claims 10 to 12, an angiogenesis activator, and a cytolytic compound, in particular a toxin.

19. Process for preparing the anti-idiotypic antibodies of claim 15, directed against monoclonal antibodies themselves directed against endothelial cells with an angiogenic phenotype, said process being characterized in that it comprises the following stages:

– immunization of an animal by injection of monoclonal antibodies according to claim 10,

– fusion between myelomas of an animal and splenocytes of an animal, in order to obtain hybridomas,

– culture of the hybridomas thus obtained,

– cloning of hybridomas, chosen from those obtained in the preceding stage and secreting antibodies directed against the abovementioned monoclonal antibodies, used for the immunization, said monoclonal antibodies being directed against cells with an angiogenic phenotype, and

– verification of the inhibition properties of the abovementioned antibodies vis-à-vis the function of activation or inhibition of the angiogenesis of the antibodies

according to claim 10, in particular using the proliferation and/or migration and/or *in vitro* angiogenesis test.

20. Anti-anti-idiotypic antibodies directed against endothelial cells with an angiogenic phenotype according to claim 6, characterized in that they are capable of activating or inhibiting angiogenesis.

21. A process for preparing the anti-anti-idiotypic antibodies of 20, directed against endothelial cells with an angiogenic phenotype, said process being characterized in that it comprises the following stages:

– immunization of an animal by injection of anti-idiotypic antibodies according to claim 15,

– fusion between myelomas of an animal and splenocytes of an animal in order to obtain hybridomas,

– culture of the hybridomas thus obtained,

– cloning of hybridomas, chosen from those obtained in the preceding stage and secreting anti-anti-idiotypic antibodies directed against cells with an angiogenic phenotype, and

– verification of the properties of inhibition or activation of the angiogenesis of the abovementioned anti-anti-idiotypic antibodies, in particular using the proliferation and/or migration and/or *in vitro* angiogenesis test.

22. A pharmaceutical composition, characterized in that it contains, as active ingredient, an angiogenesis inhibitor, chosen from an antibody according to one of claims 10 to 12, an anti-idiotypic antibody according to claim 15, a Fab fragment according to claim 16, or a complex according to claim 17, in combination with a pharmaceutically acceptable vector, said pharmaceutical composition being capable of being administered at a rate of approximately 0.01 to approximately 20 mg/kg/injection.

23. A vaccine composition, characterized in that it comprises, as active ingredient a monoclonal antibody according to one of claims 10 to 12, or an anti-idiotypic antibody according to claim 15, or Fab fragments according to claim 16, or an

anti-anti-idiotypic antibody according to claim 20, in combination with a pharmaceutically acceptable adjuvant.

24. The use of an angiogenesis inhibitor, chosen from an antibody according to one of claims 10 to 12, an anti-idiotypic antibody according to claim 15, a Fab fragment according to claim 16, or a complex according to claim 17, or an anti-anti-idiotypic antibody according to claim 20, for preparing a medicament intended for the treatment of pathologies requiring inhibition of endothelial proliferation, in particular within the framework of the following pathologies: cancers, muscle degeneration linked with age, diabetic retinopathies, rheumatoid polyarthritis, angiomas, angiosarcomas, in particular Castelman's disease and Kaposi's sarcoma.

25. The use of an angiogenesis inhibitor, chosen from an antibody according to one of claims 10 to 12, an anti-idiotypic antibody according to claim 15, a Fab fragment according to claim 16, or a complex according to claim 17, or an anti-anti-idiotypic antibody according to claim 20, for preparing a medicament intended for the treatment of pathologies requiring the inhibition of endothelial activation, in particular within the framework of the following pathologies: allograft and xenograft rejection, acrocyanosis, sclerodermas, or within the framework of the preparation of grafts between removal and the transplantation.

26. The use of an angiogenesis activator, in particular an antibody according to one of claims 10 to 12, an anti-idiotypic antibody according to claim 15, a Fab fragment according to claim 16, or an anti-anti-idiotypic antibody according to claim 20, for preparing a medicament intended to promote cicatrization in particular within the framework of injuries, tissue reconstruction in particular within the framework of muscle and cutaneous grafts during reconstructive and cosmetic surgery, ovarian induction, reperfusion of ischemic areas during arteritis of the lower limbs or myocardial infarction.